A Research Roundtable

In summer of 2023, Mercy Research sat down with three of our Mercy physician researchers — Dr. Jay Carlson, Dr. Damon Broyles and Dr. Gautum Agarwal — to discuss the ministry's emphasis on population health and preventive care and how it fits into Mercy's mission.

This conversation has been edited for brevity.

Mercy Research: *Can we begin by getting your thoughts on the ministry's direction in the areas of preventive medicine and population health?*

Dr. Broyles: My background as a family medicine doctor informs my interest in population health. I'm excited about using broad-based analytics and technology to build a population health strategy. And the precision medicine effort that Dr. Carlson has spearheaded is part of a vision that keeps questions of equity and access in the forefront of our efforts. I'm absolutely thrilled that that's the realm we're moving into.

Dr. Carlson: Leadership has put the wind in our sails and kept us moving forward with this. Although we have the passion, we've got to have the support of the leadership team in order to get started. Mercy's uniqueness in being able to do this is that we have petabytes of data on both inpatient and outpatient care. Many health systems have great inpatient data, but very limited outpatient data. We have both sides of the spectrum as well as a large primary care database that puts us in a unique situation for managing these large patient populations.

Mercy Research: *Can you talk about how these efforts align with Mercy's strategic plans?*

Dr. Carlson: Our 2025 strategic goals specifically revolve around precision medicine — the concept of the right care for the right patient at the right time. That's behind so many of the different efforts that are underway here. There are very, very few health systems that are doing broad population health or hereditary cancer screening, for instance, although the data and the evidence-based guidelines are clearly there. There's just not anybody who has put together a comprehensive plan like Mercy has.

Mercy Research: *What are some of these initiatives?*

Dr. Carlson: One of our greatest opportunities for population health and precision medicine involves screening for hereditary cancers. And from research that's been done in the past, we have good evidence-based guidelines from the National Comprehensive Cancer Network (NCCN) that tell us which individuals are at higher risk, based on heredity.

Germline testing gives us guidance as to who should have increased surveillance, prophylactic surgeries, medications or different things that would prevent cancer altogether or reduce the risk. As a team, we're very close to pushing that vision out. I hope to screen 100,000 patients for hereditary cancers during the next fiscal year.

Dr. Agarwal: The first thing that a patient thinks when they're diagnosed, whether it's high blood pressure or something as severe as cancer, is: *why did I get this disease?* And then: *what treatment am I going to get? And how is this going to affect my quality of life?*

To answer these questions, we need data. Precision medicine requires big data sets. Our new partnership with the Mayo Clinic will give us these larger population level data sets to analyze and come up with solutions. We're looking at whole genome sequencing and doing specific sequencing of genes that are responsible for diseases like chronic kidney disease and, as Dr. Carlson mentioned, hereditary cancers.

And so when that patient asks "why?", we can answer by saying: *based on the genomic tests, you have this specific mutation and this is probably why you got this disease.* We can also say: *based upon the pattern of genes, this is the treatment you should get.* Knowing the genomic profile of someone regarding a disease they're going to get, or might get, lends itself to a very specific therapy, so we'll have fewer side effects of therapy and better responses to it. All of that helps patients live better and longer.

Dr Broyles: That's an important point. We have many patients on multiple medications. Now we can leverage pharmacogenomics, which is understanding how the patient's genotype will affect how they react to a drug — how they metabolize it, what their reaction to interactions between different drugs will be. Historically, we dealt in trial and error and educated guesses. Now we're dealing with a totally different calculus — we have a level of precision that allows us to skip certain drugs, knowing that we're going to have a much higher likelihood of a beneficial response with other treatments. That has huge benefits.

IMPLEMENTING ADVANCES

Mercy Research: *How would this be implemented at the primary care doctor level?*

Dr. Agarwal: We think about how it's going to affect the patient, but we also think about how it's going to affect the providers in our entire Mercy community. We can't just roll it out without educating our providers. MCED (Multi Cancer Early Detection), our first program, was a good example. We had 12 to 15 different training sessions for all physicians.

Dr. Broyles: A lot of the technologies we're currently developing will come to the forefront because this is an area where there's going to be just exponential growth of capability. One of the most significant questions about how we roll out the technology and make it available is how to eliminate disparities in terms of where the technology is available.

We've partnered with the Mercy ministry's change management team to show Mercy clinicians why these technologies are helpful and the science that underpins them. Communicating the "why" and then the "how" is a part of precision medicine that will continue to be really important going forward. To Dr. Carlson's point about the germline mutation analysis at scale, the more patients we find with mutations, the more that patients will benefit from MCED. But we won't have buy-in from clinicians if our message to them is: *hey, now that you know about this, figure out how to deploy it on your own.*

Dr. Carlson: We've got to have multiple pathways for access because providers face so many different things, whether it's through Mercy.net, E-check-ins or a QR code scan in the office. We've been impressed with our direct-to-patient marketing for these initiatives. Our population is getting more and more educated in this area. When we market to patients, interest in Multi Cancer Early Detection just skyrockets.

A FOCUS ON MISSION

Mercy Research: *Dr. Broyles mentioned health inequities. Could you talk about closing the gap in access and the moral imperative behind that, and how this fits with Mercy's mission of bringing care to where it's needed?*

Dr. Carlson: I'll speak to charity care and our mission. As an example, we have a process that provides MCED testing at no cost to a small subset of patients with proven financial constraints who are at ultra-high risk but who could never afford the testing.

Dr. Broyles: The idea of doing the most good for the largest number of people is innate in the DNA of Mercy. You see it in the work of the providers, the clinical care teams, the executives. It's just a fundamental tenet and rationale for why we do what we do.

I'd like to add that a focus on preventing illness can often spawn all kinds of very unique and creative ways to solve problems upstream. And it's very aligned with what our foundress Catherine McAuley meant when she said: *go out and see where the source of the problem exists before someone shows up on your doorstep*. Be proactive; have a bias for action. And there's research being done about other things as well. What if we were to do address something like food insecurity? How could that head off congestive heart failure? If we're focusing on outcomes in chronic disease management, will we see better outcomes with creative solutions that address inequities in our communities?

LESSONS OF COVID-19

Mercy Research: *One major learning from the pandemic was that people with preexisting conditions were often the hardest hit. To what extent did COVID-19 accelerate the drive toward preventive care?*

Dr. Broyles: To Mercy's credit, prior to COVID, we had really started to transition heavily into a preventive care model. COVID accelerated that transition. It was good that that we already had started to build that muscle memory. COVID brought home the fact that it's way more expensive to fix problems after they've already occurred. Having systems in place that kept people out of the hospital was aligned with what people wanted during a once-in-a-lifetime pandemic, and it remains aligned with what people wanted when we started seeing COVID volumes decline.

It was a great barometer for what the future was going to look like because the future is obviously driven by pressure from payers, who want to get to a place where we're paying for positive outcomes.

Dr. Agarwal: You know, we have patients from all walks of life at Mercy, all different states, all different types of people, whether they're black, white, Native American, Asian, Indian, rich or poor. Whatever they've been exposed to in their lives, whether it's smoking or air pollution or toxic chemicals, all these things are factors that can cause or accelerate disease. Then there are the genomic profiles, which are the things under the covers. All these factors can give us advance warning for the next pandemic.

THE POLICY FRONT

Mercy Research: *Research potentially has real-world implications for millions of people. To what extent does the research you do drive policy, specifically regarding reducing health care costs?*

Dr. Carlson: I'm not sure I'd say research drives policy, but it supports it. Research can reinforce where you're spending the resources. It says, *"This is what I think we ought to be doing, and now I've got data that supports we've made the right decision. Now it's time to double down on that effort."*

Dr. Broyles: I fully agree with that, and there are other ways to use data—you can use the data in your system to look at where you have higher rates of housing insecurity, for example. That informs the policy in a very data-centric and quantitative way. It's just so vastly different than coming to policymakers with anecdotal information. Anecdotes can be powerful, but they don't move the needle much.

Dr. Carlson: Our work is based on catching disease early, or even before it's a disease. With Multi-Cancer Early Detection (MCED), the hope is that we catch cancer in stage one. This gives us a better outcome and long-term cureability than, say, multiple surgeries followed by adjuvant chemotherapy or radiation with stage three or stage four disease. Catching cancer earlier improves outcomes and at lower cost. With hereditary cancer, for example, knowing that somebody has a genetic predisposition, say, an 80% lifetime risk for breast cancer or 40% lifetime risk for ovarian cancer, gives us the opportunity to provide prophylactic surgeries or interventions at substantially lower cost and with better outcomes than treating an advanced stage cancer that has a much worse outcome.

Dr. Agarwal: The nice thing about these genetic factors is that you can obtain them more easily than with an MRI, PET scan or CT scan. It's in your hair, your nose, blood, or cheek swab. Anyone can collect the tissue for a genetic test because it's so simple. It's not invasive. Most of the time, it doesn't even require any needles, or at most, maybe a blood draw. Most of these tests could be done at home. And because Mercy has such a good footprint, even if patients can't do it at home, they can go to a local Mercy lab and have it done there.

And that technology is only going to get cheaper and quicker. It cost somewhere between $10 to $20 billion and 15 years to sequence the first genome. Now your genome can be technically sequenced in about a week for less than a thousand dollars. When you have such a powerful a tool, that tells us so much about that patient, it's amazing.

I'll give you an example. I had a patient with bladder cancer who'd failed multiple therapies. Genome sequencing turned up an FGFR mutation. Years ago, we wouldn't have even been able to find that. But because we knew the patient had the FGFR mutation through their genomic analysis, we gave them a next-generation drug that targets the FGFR receptor and they had a complete response to their cancer. Their cancer was progressing and was in their bones and lungs. And it completely went away.

One argument genomic naysayers make is: *well, you're only saving one patient's life out of 100*. If you're that one patient, that means a lot. If you're the grandchild of that one patient, that means a lot. And when you look at three million patients at Mercy alone—that's about 30,000 people you're saving. You're saving a lot of people. And you're not just saving their life, but changing the trajectory of their life, from experiencing a potentially early, quick death to maybe surviving and living a full lifespan.

Dr. Carlson and I always talk about how, yes, a lot of these tests uncover what are considered rare genetic diseases. But there are 30 million Americans right now who have a rare genetic disease that we just don't know about. The more people you test, the less rare the disease gets.

Mercy Research: *Let me conclude by asking a personal question. What drives your motivation for this research and your population health/preventive care focus?*

Dr. Carlson: Well, I'll say my personal motivation was that my dad had five different cancers by the time he was 60. He died in 2001, before we had any of these genetic tests. There was clearly something either genetic or environmental in his exposure history that gave him five different types of cancer. Trying to understand those types of situations and leverage the current testing capabilities just seems like the right thing to do. And then when we have something like the NCCN guidelines that would allow us to identify patients at hereditary risk and usually get insurance to pay for it —you start asking: why aren't we testing 100,000 patients a year? It's taken us 20 years to get here, but this question has always been in the back of my mind.

I could tell a few other stories. I had an ovarian cancer patient whose sister had endometrial cancer and they're both my patients. As soon as the one was diagnosed with ovarian cancer, I told her sister, "You need the germline test." And they both tested positive for a BRCA-2 mutation. They became champions to educate everybody in their family. They contacted relatives out in California who were distant cousins, who unfortunately told them that they've *known about that mutation for a long time; everybody out here has been tested and taken care of.* The education and management of the hereditary mutation in that family clearly failed my two patients.

Because of that breakdown in communication and not having coordinated efforts, my patient had extremely bad outcomes and went through horrific treatments. Most of their cancer risk could have been prevented if we had only known that they harbored a BRCA mutation. And that's what Mercy's trying to address. By doing the research and linking the data, we can affect significant changes for patients and family and do so at lower cost and with better outcomes than treating a cancer, when it occurs.

Dr. Broyles: I think about the idea of compacts. I have a compact with my patients who suffered disastrous illnesses. And we have an obligation to the memory of those who aren't with us anymore, to honor them. I think we also have a responsibility to the research scientists who worked at the bench, devoting their lifetime to understanding human physiology and the human genome and what that means from the perspective of treating disease. If we don't do this, it'd be like somebody who wrote this gorgeous symphony and they only played it for themselves on a desert island.

Dr. Agarwal: Well, using myself as an example: I just turned 41 and I've got a three-year-old. I want to be around for a long time. And I have a family history of heart attacks and strokes over multiple generations. I could be a ticking time bomb. So how would Mercy be able to detect that?

That's where Mercy is going to be phenomenal. I have so much confidence in what we've done so far and for the future because we'll pick up those phenotypic signals through our combined Mercy and Mayo platforms, where we're sharing eight to nine petabytes of information. We'll look at whole populations of data. And within those populations, we'll develop algorithms and do the research. They'll say, *okay, we looked at 300 things about Gautum Agarwal, and he has all these factors—he has a gene or a sequence of genes or proteome that shows he has a higher risk of developing heart disease*. And we can target that gene with a specific drug. Or we will get him started on an early statin.

Another option might be to use an algorithm to predict if the patient is going to develop atrial fibrillation or some other disease in the future. Through the precision medicine program, we'll be able to do these types of preventive measures and potentially save the individual from catastrophe. Maybe within the next five years, a lot of our patients will have genomic sequencing and that will detect issues that normal, traditional signals would not identify. So I look at this from the standpoint of 100,000 Gautum Agarwals, who are 41 and want to stay alive a long time.

I think Mercy actually is ahead of most medical systems in the nation, including academic medical centers, in being able to apply not only precision medicine when it comes to genomics, but also large-scale population level data sets to be able to develop and deploy algorithms to better the lives of our patients.